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(58) Field of Search

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(54) Topical preparation for relief of erectile dysfunction

(57) This invention relates to a topical preparation for the relief of erectile dysfunction containing [a] aminophylline; [b] co-dergocrine mesylate; [c] isosorbide dinitrate; [d] at least one compound capable of releasing and/or donating and/or carrying nitric oxide; e.g. L-arginine and optionally [e] testosterone.

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TOPICAL PREPARATION FOR RELIEF OF ERECTILE DYSFUNCTION

The present invention relates to pharmaceutical preparations for the relief of erectile dysfunction.

5 The use of mechanical and/or pharmaceutical preparations for the treatment of impotence in men is well known. However these methods have often been clumsy and mechanical or cold blooded and anxiety producing. The present invention concerns a preparation that is applied
10 directly to the penis.

 According to the present invention a topical preparation for the relief of erectile dysfunction contains [a] aminophylline; [b] co-dergocrine mesylate; [c] isosorbide dinitrate; [d] at least one compound capable of
15 releasing and/or donating and/or carrying nitric oxide; and optionally [e] testosterone.

 According to the present invention the topical preparation can be supplied in the form of a cream, gel or spray for application to the penis before sexual activity.
20 Thus the mentioned active components can be carried in a water-based cream or jelly such as KY jelly.

 A preferred embodiment of the invention is a medicated condom, in which a preparation according to the invention is contained within a prophylactic sheath, e.g. as an internal
25 coating. When the condom is worn the active ingredients of the preparation are held in contact with the penis all the time; other benefits are the retention of blood within the

penis due to the condom and the prevention of rubbing off of the preparation on the sexual partner.

5 The preparation according to the invention can generate high concentrations of NO in the genital tract of both men and women, and this can have both spermicidal and bacteriocidal (and even virocidal) effects to make for safer sex.

10 A preferred component [d] for use in the invention is L-arginine, which is the natural substrate for all three forms of the NOS (Nitric Oxide Synthase) enzyme in the body; it also has the advantages that it is a natural product which is often taken in large amounts by mouth, and is easily and cheaply available.

15 Other compounds suitable for component [d] include sodium nitrite, amyl nitrite, glyceryl trinitrate, sodium nitroprusside, 3- morpholinosydonimine (SIN-1), S-nitroso-N-acetyl-D,L-penicillamine (SNAP), S-nitrosoglutathione (SNOG), and the nitroxyl releaser N-acetyl-N-acetoxy-4-chlorobenzenesulphonamide (NANAC).

20 The above compounds for use as or in component [d] may be present singly or in any combination of two or more.

25 A suitable concentration of component [d] in the preparation is 0.01-5% w/v, e.g. about 1% w/v. All percentages herein are calculated as weight in grams per 100 ml of the total preparation.

 In preparations according to the invention any form of testosterone as component [e] (when present) may be used.

A preferred example contains dihydrotestosterone (DHT). Testosterone, and especially DHT, has a local effect, sensitising the penis and aiding NO generation, and in higher concentrations is absorbed systemically, contributing
5 to the general actions of testosterone given by other routes. These general actions include enhancement of libido and potency.

A suitable concentration of component [e], when present, is up to 0.5 or 5% w/v (g/100 ml).

10 Compound [c], isosorbide dinitrate, is absorbed topically and will general nitric oxide;; it is suitably present in a proportion of 0.1 to 1%, e.g. about 0.25%, g/100 ml. Components [a] and [b] can improve blood supply to the penis to facilitate erection. Component [a] is
15 suitably present in a concentration of 0.5 to 5%, e.g. about 3%, g/100 ml. Component [b] is suitably present in a concentration of 0.1 to 2%, e.g. about 0.05%, g/100 ml.

One preferred preparation according to the invention has the composition (A) :

20	component [d]	1%
	Aminophylline	3%
	Mesylated co-dergocrine	0.05%
	Isosorbide dinitrate	0.25%
	KY jelly (excipient)	balance

25 Another preferred preparation according to the invention has the above composition (A) with up to 0.5g/100 ml of testosterone (e.g. DHT) also included.

CLAIMS :

1. A topical preparation for the relief of erectile dysfunction containing [a] aminophylline; [b] co-dergocrine mesylate; [c] isosorbide dinitrate; [d] at least one
5 compound capable of releasing and/or donating and/or carrying nitric oxide; and optionally [e] testosterone.
2. A preparation according to claim 1 containing the testosterone component comprising dihydrotestosterone (DHT).
3. A preparation according to claim 1 or 2 wherein
10 component [d] comprises L-arginine.
4. A preparation according to claim 1 or 2 wherein component [d] is selected from L-arginine, sodium nitrite, amyl nitrite, glyceryl trinitrate, sodium nitroprusside, 3-morpholinositydonimine (SIN-1), S-nitroso-N-acetyl-D,L-
15 penicillamine (SNAP), S-nitrosoglutathione (SNOG) and the nitroxyl releaser N-acetyl-N-acetoxy-4-chlorobenzenesulphonamide (NANAC).
5. A preparation according to any preceding claim containing 0.5-5% of [a], 0.01-0.2% of [b], 0.1-1% of [c],
20 0.01-5% of [d], and 0 to 0.5% of [e], all percentages being calculated as weight g/100 ml of the preparation.
6. A preparation according to any preceding claim containing 3% of [a], 0.05% of [b], 0.25% of [c] and 1% of [d], all percentages being calculated as weight g/100ml of
25 the preparation.

7. A preparation according to any preceding claim in the form of a cream, gel or spray.

8. A preparation according to any preceding claim carried within a condom or prophylactic sheath.